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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/397,846	09/17/1999	SCOTT R. PRESNELL	98-54	9291

7590 06/16/2003

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EXAMINER
ROMEO, DAVID S

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 06/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/397,846	PRESNELL ET AL.	
	Examiner	Art Unit	
	David S Romeo	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 May 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) *1-5,10 and 11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-11* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-11 are pending.

Applicant's election without traverse of group II, claims 6-9, in Paper No. 7 is acknowledged.

Applicant's election without traverse of the species SEQ ID NO: 3 in Paper No. 10 is acknowledged.

Claims 1-5, 10, 11 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 7.

In a telephone conversation with Michelle Johnson on June 1, 2003 examiner Romeo indicated that he wanted to revise the restriction requirement mailed December 18, 2000 (Paper No. 4) such that SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 9, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, and SEQ ID NO: 22 were separate inventions rather than an election of species. In response Ms. Johnson elected SEQ ID NO: 3. In view of examination of the application, the restriction requirement is re-cast as follows.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claim(s) 6-9, to the extent that they are drawn to a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, a polypeptide comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 2, and a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, and SEQ ID NO: 22, classified in class 530, subclass 350.

II. Claim(s) 6-9, to the extent that they are drawn to a polypeptide comprising the amino acid sequence of SEQ ID NO: 3, a polypeptide comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 3, and a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, classified in class 530, subclass 350.

III. Claim(s) 6-9, to the extent that they are drawn to a polypeptide comprising the amino acid sequence of SEQ ID NO: 4, a polypeptide comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 4, and a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, classified in class 530, subclass 350.

IV. Claim(s) 6-9, to the extent that they are drawn to a polypeptide comprising the amino acid sequence of SEQ ID NO: 5, a polypeptide comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 5, and a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, classified in class 530, subclass 350.

V. Claim(s) 6-9, to the extent that they are drawn to a polypeptide comprising the amino acid sequence of SEQ ID NO: 13, a polypeptide comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 13, and a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 19, classified in class 530, subclass 324.

VI. Claim(s) 6-9, to the extent that they are drawn to a polypeptide comprising the amino acid sequence of SEQ ID NO: 14, a polypeptide comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 14, and a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, classified in class 530, subclass 326.

VII. Claim(s) 6-9, to the extent that they are drawn to a polypeptide comprising the amino acid sequence of SEQ ID NO: 15, a polypeptide comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 15, and a polypeptide comprising

an amino acid sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, classified in class 530, subclass 324.

VIII. Claim(s) 6-9, to the extent that they are drawn to a polypeptide comprising the amino acid sequence of SEQ ID NO: 19, a polypeptide comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 19, and a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, classified in class 530, subclass 324.

IX. Claim(s) 6-9, to the extent that they are drawn to a polypeptide comprising the amino acid sequence of SEQ ID NO: 20, a polypeptide comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 20, and a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 19, classified in class 530, subclass 326.

X. Claim(s) 6-9, to the extent that they are drawn to a polypeptide comprising the amino acid sequence of SEQ ID NO: 21, a polypeptide comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 21, and a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, classified in class 530, subclass 324.

XI. Claim(s) 6-9, to the extent that they are drawn to a polypeptide comprising the amino acid sequence of SEQ ID NO: 22, a polypeptide comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 22, and a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 19, classified in class 530, subclass 327.

XII. Claim(s) 6-9, to the extent that they are drawn to a polypeptide comprising the amino acid sequence of SEQ ID NO: 9, a polypeptide comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 9, and a polypeptide comprising the amino acid sequence of SEQ ID NO: 12, classified in class 530, subclass 350.

XIII. Claim(s) 6-9, to the extent that they are drawn to a polypeptide comprising the amino acid sequence of SEQ ID NO: 12, a polypeptide comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 12, and a polypeptide comprising the amino acid sequence of SEQ ID NO: 9, classified in class 530, subclass 350.

XIV. Claim(s) 6-9, to the extent that they are drawn to a polypeptide comprising the amino acid sequence of SEQ ID NO: 17, a polypeptide comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 17, and a polypeptide comprising the amino acid sequence of SEQ ID NO: 18, classified in class 530, subclass 350.

XV. Claim(s) 6-9, to the extent that they are drawn to a polypeptide comprising the amino acid sequence of SEQ ID NO: 18, a polypeptide comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 18, and a polypeptide comprising the amino acid sequence of SEQ ID NO: 17, classified in class 530, subclass 350.

The inventions are distinct, each from the other because of the following reasons:

The following pairwise combinations of products are independent and distinct, wherein neither member of a pair is required for the production or use of the other, and wherein each of the pair can be manufactured independently of the other and used for independent and distinct purposes: I and each of II-XV; II and each of III-XV; III and each of IV-XV; IV and each of V-XV; V and each of VI-XV; VI and each of VII-XV; VII and each of VIII-XV; VIII and each of IX-XV; IX and each of X-XV; X and each of XI-XV; XI and each of XII-XV; XII and each of XIII-XV; XIII and each of XIV-XV; XIV and XV.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

Because these inventions are distinct for the reasons given above and the searches required for at least 90% identity to each of the polypeptides are not coextensive, restriction for examination purposes as indicated is proper.

During a telephone conversation with Michelle Johnson on June 1, 2003 a provisional election was made with traverse to prosecute the invention of SEQ ID NO: 3, claims 6-9. In view of the fact that group II, claims 6-9, comprises both SEQ ID NO: 3 and 90% identical to

SEQ ID NO: 3, group II is being examined on the merits. Affirmation of this election must be made by applicant in replying to this Office action. Claims 6-9 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), to the extent that they are drawn to a non-elected invention..

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 6 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are directed to or encompass a polypeptide comprising an amino acid sequence at least 90% identical to SEQ ID NO: 3. There is no functional limitation in the claims. The claims are broad because they do not require the claimed polypeptide to be identical to the disclosed sequences and because the claims have no functional limitation. The specification lacks guidance for making polypeptides at least

90% identical to SEQ ID NO: 3 that retain a specific function of SEQ ID NO: 2. There are no working examples of polypeptides less than 100% identical to the polypeptide SEQ ID NO: 2 or the mature forms thereof. The skilled artisan would not know how to use non-identical polypeptides unless they possessed a specific activity or function. The specification does not provide guidance for using polypeptides related to (i.e., at least 90% identical) but not identical to at least SEQ ID NO: 3 which do not have a specific activity or function. The claim encompasses an unreasonable number of inoperative polypeptides, which the skilled artisan would not know how to use. Moreover, there is a lack of predictability in the art. Predicting structure, hence function, from primary amino acid sequence data is extremely complex and there doesn't exist an efficient algorithm for predicting the structure of a given protein from its amino acid sequence alone. See Bowie (x14) page 1306, column 1, full paragraph 1, or Ngo (y14) page 433, full paragraph 1, and page 492, full paragraph 2.

In view of the breadth of the claims, the limited amount of direction and working examples provided by the inventor, the unpredictability in the art and the quantity of experimentation needed to make or use the invention based on the content of the disclosure, it would require undue experimentation for the skilled artisan to make and/or use the full scope of the claimed invention.

Claims 6 and 7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to polypeptides having at least 90% sequence identity with SEQ ID NO: 3 and to polypeptides comprising fragments (SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, and SEQ ID NO: 22) of SEQ ID NO: 2. The claims do not require that the polypeptide possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polypeptides that is defined only by some level of sequence identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Further the claims embrace any and/or all polypeptides having any and/or all functionality conferred by any and/or all unspecified and unlimited structure in addition to the structure of the specific fragment. A description of SEQ ID NO: 3 is not a description of any and/or all polypeptides having any and/or all functionality conferred by any and/or all unspecified and unlimited structure. Accordingly, in the absence of sufficient recitation of distinguishing identifying

characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, or SEQ ID NO: 5, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Therefore, only isolated polypeptides consisting of the amino acid sequence set forth in SEQ ID NO: 13, SEQ ID

NO: 14, SEQ ID NO: 15, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 6-9 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The present specification provides a Ztgfβ-9 polypeptide (SEQ ID NO: 2), whose sequence was deduced from the conceptual translation of the human Ztgfβ-9 cDNA (SEQ ID NO: 1). Ztgfβ-9 is homologous to two members of the IL-17 family. The four conserved cysteines are predicted to be involved in forming a cysteine-knot-like protein fold that is related to that found in the TGF-β proteins. See page 68, full paragraph 2.

However, one skilled in the art recognizes that although structural similarity can serve to classify a protein as related to other known proteins this classification is insufficient to establish a function or biological significance for the protein because ancient duplications and rearrangements of protein-coding segments have resulted in complex gene family relationships. Duplications can be tandem or dispersed and can involve entire coding regions or modules that correspond to folded protein domains. As a result, gene products may acquire new specificities, altered recognition properties, or modified functions. Extreme proliferation of some families

within an organism, perhaps at the expense of other families, may correspond to functional innovations during evolution. See Henikoff (u14), page 609, Abstract. Accordingly, one skilled in the art would not accept mere homology as establishing a function of protein because gene products may acquire new specificities, altered recognition properties, or modified functions. Rather, homology complements experimental data accumulated for the homologous protein in understanding the homologous protein's biological role. Although, the presence of a protein module in a protein of interest adds potential insight into its function and guides experiments, insight into the biological function of a protein cannot be automated. However, homology can be used to guide further research. See Henikoff (u14), paragraph bridging pages 613-614, through page 614, paragraph bridging columns 1-2.

Ztgfβ-9 is identical in amino acid sequence to IL-17D, as indicated in the following entry from the SPTREMBL_21 database entry below:

```
Q8TAD2
ID   Q8TAD2      PRELIMINARY;      PRT;   202 AA.
AC   Q8TAD2;
DT   01-JUN-2002 (TrEMBLrel. 21, Created)
DT   01-JUN-2002 (TrEMBLrel. 21, Last sequence update)
DT   01-JUN-2002 (TrEMBLrel. 21, Last annotation update)
DE   Interleukin 27 precursor (IL17D precursor).
GN   IL27.
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   TISSUE=ENTIRE BRAIN;
RA   Hadj-Slimane R., Bobe P.;
RT   "Interleukin 27 (IL27): a newly identified cytokine.";
RL   Submitted (FEB-2002) to the EMBL/GenBank/DDBJ databases.
RN   [2]
RP   SEQUENCE FROM N.A.
RA   Hromas R.A., Starnes T.T.;
RT   "IL-17D, A Novel Member of the IL-17 Family, Stimulates Cytokine
RT   Production and Inhibits Hematopoiesis.";
RL   Submitted (FEB-2002) to the EMBL/GenBank/DDBJ databases.
DR   EMBL; AY078238; AAL86911.1; -.
DR   EMBL; AF479775; AAM12734.1; -.
KW   Signal.
FT   SIGNAL       1      5       POTENTIAL.
SQ   SEQUENCE   202 AA;  21893 MW;  D171C5FB2DD039C3 CRC64;

  Query Match            100.0%;  Score 1089;  DB 4;  Length 202;
  Best Local Similarity  100.0%;  Pred. No. 4.3e-99;
  Matches  202;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MLVAGFLLALPPSWAAGAPRAGRRPARPRGCADRPEELLEQLYGRLAAGVLSAFHHTLQL 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MLVAGFLLALPPSWAAGAPRAGRRPARPRGCADRPEELLEQLYGRLAAGVLSAFHHTLQL 60

Qy         61 GPREQARNASCPAGGRPADRRFRPPTNLRSVSPWAYRISYDPARYPRYLPEAYCLCRGCL 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 GPREQARNASCPAGGRPADRRFRPPTNLRSVSPWAYRISYDPARYPRYLPEAYCLCRGCL 120
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Qy      121 TGLFGEEDVRFRSAPVYMPTVVLRRTPACAGGRSVYTEAYVTIPVGCTCVPEPEKDADSI 180
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      121 TGLFGEEDVRFRSAPVYMPTVVLRRTPACAGGRSVYTEAYVTIPVGCTCVPEPEKDADSI 180

Qy      181 NSSIDKQGAKLLLGPNDAPAGP 202
            ||||||||||||||||||||||
Db      181 NSSIDKQGAKLLLGPNDAPAGP 202
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Although the present specification discloses structural similarity to the IL-17 family, the specification fails to make a specific and substantial assertion of utility based upon this structural similarity. Further, the IL-17 family has no sequence similarity to any other known cytokines (Starnes (v14) at page 642, left column, full paragraph 1). The IL-17 family of proteins and their corresponding receptors represent a unique family of cytokines that is not yet fully understood (Starnes (v14) at page 642, right column, full paragraph 2). IL-17D does not appear to have the ability to stimulate the proliferation of immune cells on its own, but it does have the ability to stimulate the production of other cytokines from target tissues such as endothelial cells. This is similar to other members of the IL-17 family, which are thought to indirectly modulate the immune response by regulating cytokine production. The cytokines induced by IL-17D, such as IL-6, IL-8 and GM-CSF, are similar to those induced by other IL-17 family members (Starnes (v14) at page 645, left column, full paragraph 2). However, IL-17D is preferentially expressed in skeletal muscle, brain, adipose tissue, heart, lung, and pancreas, which is unusual for IL-17 family members. For example, IL-17F is only expressed in activated monocytes and activated CD4+ T cells (11). It is possible that IL-17D plays a role in local immune responses that might occur in those tissues, perhaps after local structural damage such as in trauma, myocardial infarction, or stroke. It is also possible that IL-17D could be important in the growth or repair of those tissues after such structural damage. See Starnes (v14) at page 645, left column, full paragraph 3). IL-17D also suppresses the proliferation of myeloid progenitors in colony

formation assays. This is in contrast to its ability to induce the production of GM-CSF, which stimulates progenitor proliferation (Starnes (v14) at page 645, paragraph bridging left and right columns). This is also in contrast to IL-17, which can induce fibroblasts to secrete IL-6 and G-CSF, which can induce proliferation and differentiation of $CD34^+$ hemopoietic progenitors. IL-17 can also stimulate granulopoiesis in vivo and induce murine stem cells to rescue lethally irradiated mice, suggesting its importance in hemopoiesis (Starnes (v14) at page 642, right column, full paragraph 1).

The cystine knot motif is characteristic of a structural superfamily growth factors comprising NGF, TGF-β, PDGF, and v-Sis. See McDonald (w14), page 421, Table 1. Although these growth factors share structural features in common, their biological roles are distinct. See McDonald (w14), page 423, left column, full paragraph 3.

This evidence shows that the members of the IL-17 family and that proteins possessing a cysteine-knot-like protein fold do not share a specific, substantial functional attribute or utility, despite having structural features in common, and that membership in the IL-17 family or possession of a cysteine-knot-like protein fold does not impute a specific and substantial utility to the Ztgfβ-9 polypeptide of the present application

The specification asserts that Ztgfβ-9 has antiviral activity (page 4, full paragraph 1). Specifically, the specification asserts that the Ztgfβ-9 inhibits adenovirus growth (pages 75-76, Example 10). Transfection of Ztgfβ-9 adenoviral genomes into cells resulted in very small viral plaques, which did not expand. After 2-3 rounds of viral replication a rapidly growing virus population was obtained. Although, the virus that results from this amplification still contained the Ztgfβ-9 sequence, no Ztgfβ-9 protein was produced. The specification concludes that virus

replication was clearly inhibited. Although it may be clear that virus replication was inhibited, it is not so clear that this inhibition was due to Ztgfβ-9 protein production because no evidence is provided that Ztgfβ-9 protein was produced initially. If the Ztgfβ-9 was produced initially it is unclear if the Ztgfβ-9 produced inhibited viral production or if the amplification selected for a well growing virus, whereas the initial viral stock grew poorly.

The specification at page 4, full paragraph 1, asserts that Ztgfβ-9 may be used to regulate the proliferation, differentiation, and apoptosis of neurons, glial cells, lymphocytes, hematopoietic cells and stromal cells. However, the specification does not disclose a specific regulation and whether such regulation would be considered advantageous or detrimental. These asserted utilities are also not substantial, because significant further research would have to be conducted to determine the nature of such proliferation, differentiation, and apoptosis.

The specification asserts at page 69, full paragraph, that based upon the expression of Ztgfβ-9 in brain and spinal cord, Ztgfβ-9 can be used to treat a variety of neurodegenerative diseases. However, the specification does not disclose whether such expression would be considered advantageous or detrimental in a particular neurodegenerative disease. In the absence of this information significant further research would have to be conducted to determine how Ztgfβ-9 could be used to treat a neurodegenerative disease. These asserted utilities are thus not substantial.

The specification at page 67, full paragraph 1, asserts that the present invention provides reagents that will useful in diagnostic applications. However, in order for a polypeptide to be useful, as asserted, for diagnostic applications, there must be a well-established or disclosed correlation or relationship between the claimed polypeptide and a particular diagnosis. If a

molecule is to be used as a surrogate for a disease state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polypeptide to be used in a diagnostic manner. Many proteins are expressed in normal tissues and diseased tissues. Therefore, one needs to know, e.g., that the claimed polypeptide is either present only in diseased tissue to the exclusion of normal tissue or is expressed in higher levels in diseased tissue compared to normal tissue (i.e. overexpression). Evidence of a differential expression might serve as a basis for use of the claimed polypeptide as diagnostics for diseases.

The instant situation is directly analogous to that which was addressed in Brenner v. Manson, 148 U.S.P.Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility. The court held that:

The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to

engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion.

The instant application has failed to provide guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a specific and substantial utility. The proposed uses of the claimed invention are simply starting points for further research and investigation into potential practical uses of the claimed polypeptide. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." Brenner v. Manson, 148 USPQ at 696.

Claims 6-9 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Information Disclosure Statement

The information in the IDS filed February 26, 2001 (Paper No. 6) has been considered to the extent possible by but a residue by residue comparison of the sequences in the IDS with the claimed sequences has not been done.

Conclusion

No claims are allowed. A polypeptide comprising the amino acid sequence of SEQ ID NO: 3, a polypeptide comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 3, and a polypeptide comprising an amino acid sequence selected from

the group consisting of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, and SEQ ID NO: 22 are free of the prior art of record.

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JUNE 14, 2003